REMARKS

Claims 1, 2, 4, 5, 7, 13-16, 19, 21, 23, 25, 26, 28-31, 33, 34, 36-42, 49-51 and 53-55 were pending. Claims 1, 2, 4, 5, 7, 13-16, 19, 21, 23, 25, 26, 28-31, 33, 34, 36-42, 51 and 53-55 are canceled herein without prejudice to their presentation in a related application. Thus, after entry of this amendment, **claims 49 and 50 will be pending**.

Claim 49 is amended herein to incorporate limitations of claims 1 and 33, and for clarity. Claim 50 is amended to replace "A method" with "The method." No new matter has been introduced by these amendments and no amendments are made to distinguish prior art.

EXAMINER INTERVIEW

Applicants thank Examiner Marvich for the courtesy of a brief telephone interview on November 18, 2009 to discuss the objection to claims 49 and 50. Examiner Marvich confirmed that amendment of claim 49 to incorporate the limitations of claim 33 would obviate the objection.

CLAIM OBJECTION

Claims 49 and 50 are objected to as comprising non-elected subject-matter. Claim 49 is re-written in independent format as required by the Office, rendering this rejection moot.

REJECTION UNDER 35 USC §102(b)

Claims 49 and 50 are rejected under 35 USC §102(b) as allegedly anticipated by Chang *et al.* (U.S. Patent No. 6,207,455). In particular, the Office alleges that Chang *et al.* teach "methods of constructing a hybrid virus wherein the envelope protein is from SIV and the transducing vector comprises a nucleotide sequence of interest and an HIV packaging signal." However, the Office has misinterpreted the teaching of Chang *et al.* In fact, there is no disclosure whatsoever in Chang *et al.* of the chimaeric viruses as presently claimed. Thus, since the Chang *et al.* reference does not teach each and every limitation of the pending claims, the claims are not anticipated.

Claim 49 is directed to a method of delivering a therapeutic or antigenic protein or peptide to an individual by administering to the individual an effective amount of a chimaeric virus (or a vector system, host cell, or pharmaceutical composition comprising the chimaeric virus) produced by culturing a host cell which comprises: (1) one or more SIV nucleic acid sequences capable of producing an SIV capsid; and (2) a vector comprising an HIV-2 packaging signal and a heterologous nucleic acid sequence. The vector is packaged in the SIV capsid to produce a chimaeric virus. In contrast, Chang *et al.* do not disclose chimaeric viral vectors with the specific features set out in the instant claims. In particular, Chang *et al.* do not teach a chimaeric virus (or a method of producing such a virus) having (1) an SIV capsid and (2) a vector encoding an HIV-2 packaging signal and a heterologous nucleic acid sequence.

Chang *et al.* relates to attenuated lentiviral vectors. Although a number of different lentiviruses are mentioned in the text, including HIV-2, FIV, SIV, CAEV, EIAV and BIV (see column 5, lines 22 to 27), Chang *et al.* only contains experimental data on HIV-1 based vector systems.

The Examiner cites column 5 and the paragraph bridging columns 5-6 as allegedly teaching a hybrid virus. However, this passage does not disclose a chimeric viral vector that comprises a heterologous nucleic acid linked to an HIV-2 packaging signal which is packaged in an SIV capsid, as described in the present application. Column 5, lines 29 to 31, of Chang *et al.* states:

> *The present invention also provides lentiviral vectors, wherein the vector comprises <u>at least a portion</u> of the recombinant lentivirus genome.* [emphasis added]

Column 5, lines 53 to 59, states:

> *In preferred embodiments, the recombinant lentivirus genome contained with the lentiviral vector is selected from the group consisting of human immunodeficiency virus type 1, human immunodeficiency virus type 2, feline immunodeficiency virus, simian immunodeficiency virus, visna maedi, caprine arthritis-encephalitis virus, equine infectious anemia virus, and bovine immune deficiency virus.*

Column 5, lines 59 to 63, go on to state:

> *...recombinant lentivirus may be recombinant HIV-1, HIV-2, SIV, or a virus comprised of portions of more than one lentiviral species (e.g., a hybrid, comprised of portions of HIV-1 and HIV-2, or HIV-1 and SIV, etc.)*

In other words, the lentiviral vector of Chang *et al.* may contain some or all of a genome from a recombinant lentivirus, which can be from any one of a number of lentiviral genomes or it may be a hybrid of sequences from different lentiviruses.

However, insofar as the Chang *et al.* recombinant lentivirus may be a hybrid, there is no disclosure in Chang *et al.* of which portions of sequence from different lentiviruses might be contained in the hybrid virus. In addition, there is no disclosure of a hybrid virus containing portions of sequence from HIV-2 and SIV.

Furthermore, it is clear from the paragraph bridging columns 5-6 that the teaching of column 5 relates to packaging vectors. All the examples of lentiviral vectors which are provided in column 5 (SEQ ID NO: 13, pHP-1, pHP-dl.2 and pHP-dl.28, pHP-VSVG, pHP-CMV, pHP-CMVdel.TAR/SD, pHP-CMV-EF1a intron, and pHP-EF) are packaging vectors, whereas transducing vectors are discussed elsewhere in Chang *et al.* (*i.e.* at column 6, line 38, to column 7, line 7). Chang *et al.* contains no disclosure of an SIV packaging vector being used to package RNA from a vector with an HIV-2 packaging signal, either in column 5 and the paragraph bridging columns 5-6 or elsewhere.

The Office also cites Example 5 at column 44, lines 1 to 11, as allegedly teaching a chimaeric virus which comprises HIV-2 packaging signals within an SIV viral capsid. However, when this passage is read in the context of the rest of Example 5 (and the rest of the specification), it is apparent that it does not teach any such chimaeric virus.

Example 5 is entitled "Construction of HIV-2 and SIV vectors". This title is indicative that the disclosure of Example 5 relates to HIV-2 vectors and SIV vectors and does not extend to

chimaeric vectors containing sequences from both HIV-2 and SIV. Furthermore, Example 5 is written in the present tense and is therefore entirely prophetic. The experiments described in Example 5 are therefore speculative and have not actually been carried out by the authors of Chang *et al.*

The authors of Chang *et al.* state at column 43, lines 50 to 52:

> *Based upon the experiments conducted during development of the HIV-1 vector system, HIV-2 and SIV vector systems are developed (pH2P and pSIVP).*

In other words, the authors propose developing two packaging vector systems (pH2P and PSIVP), which are based on HIV-2 and SIV respectively and which would be produced in an analogous manner to the HIV-1 vectors that are described in earlier examples. The earlier experimental examples describing the development of the HIV-1 system do not refer to chimaeric viruses, and it follows that Example 5, which is based on these earlier examples, does not relate to chimaeric viruses either. This is confirmed in column 43, lines 52 to 53, which refer to "a lentiviral vector based on HIV-2 or SIV." It is clear from this choice of wording that chimaeric vectors which combine both HIV-2 and SIV are not envisaged by the authors of Chang *et al.*

The authors of Chang *et al.* briefly mention cross-packaging at column 43, line 66, to column 44, line 2:

> *Previous studies suggested that SIV or HIV-2 genomes can be assembled into the HIV-1 particles, indicating that the packaging signals of SIV or HIV-2 can be recognized by HIV-1 nucleocapsids.*

However, no experimental examples of cross-packaging are provided Chang *et al.* and there is no mention of cross-packaging in lentiviral capsids other than HIV-1. As explained below, it not always possible to package RNA from one lentivirus in the capsid of another. In fact, the data in Applicants' specification shows that Chang *et al.* is incorrect in suggesting that HIV-1 capsids package SIV genomes (see Figure 1 of the instant specification).

The authors of Chang *et al.* go on to state at column 44, lines 2 to 11:

To construct a lentiviral 'transducing vector' based on HIV-2 or SIV, a construct similar to the pTVA vector is made which contains the SIV or HIV-2 packaging signals (from 3' of the PBS to the extended gag sequences). These HIV-2 and SIV transducing vectors (pTV2 and pTVS) are first tested in co-transfection experiments using pH2P or pSIVP. The transduction efficiency is compared to the HIV-1 vector constructs carrying the reporter gene lacZ.

One of ordinary skill in the art would understand this passage as teaching that the recombinant HIV-2 transducing vector pTV2 is tested with the HIV-2 packaging vector pH2P and the recombinant SIV transducing vector pTVS is tested with the SIV packaging vector pSIVP. There is nothing in this passage which suggests the use of the HIV-2 packaging vector with the SIV transducing vector (which in fact would not work) or any other cross packaging system.

One of ordinary skill in the art would not understand the above passage as teaching the use of HIV-2 packaging signals in SIV capsids. This interpretation is inconsistent with the wording of the passage and is incompatible both with the rest of Example 5 and the rest of the Chang *et al.* specification, which is totally silent about cross-packaging. There is neither exemplification nor disclosure anywhere in Chang *et al.* of a cross-packaging system in which one type of lentivirus packages RNA from another.

The Office further cites claims 4 and 8 of Chang *et al.* Claim 4 of Chang *et al.* relates to the use of SIV as a packaging vector. Claim 8 refers to lentiviral Env proteins. However, there is no disclosure, either individually or in combination in claims 4 and 8 (or any other claims) of the use of HIV-2 packaging signals in SIV viral capsids.

Applicants' use of HIV-2 packaging signals in SIV capsids is not an arbitrary combination. The present inventors have identified a non-reciprocal packaging relationship between the lentiviruses HIV-1, HIV-2 and SIV. For example, HIV-1 packages HIV-2 RNA but

not SIV RNA (Figure 1), SIV packages HIV-2 RNA but not HIV-1 RNA (Figure 2) and HIV-2 does not package either HIV-1 or SIV RNA (Figure 3). Non-reciprocity of cross-packaging (for example between HIV-2 and SIV) is highly advantageous for the production of viral vectors because it prevents dangerous replicative viruses being generated through recombination events.

By contrast, Chang *et al.* addresses the problem of recombination events in a completely different way: by mutating key sequences within the lentiviral vector. Chang *et al.* contains no disclosure or suggestion that cross-packaged lentiviruses might be used to address this problem or that the packaging of heterologous nucleic acid linked to an HIV-2 packaging signal in an SIV capsid would be an appropriate solution.

In summary, there is no teaching or suggestion in Chang *et al.* of chimaeric viral vectors which comprise heterologous nucleic acid linked to HIV-2 packaging signals contained within an SIV viral capsid, as required in the instant claims.

Claims 49 and 50 are therefore not anticipated by Chang *et al.* Accordingly, Applicants request withdrawal of this rejection under 35 USC §102(b).

CONCLUDING STATEMENT

It is respectfully submitted that the present claims are in a condition for allowance. Should the Examiner have further questions or comments with respect to examination of this case, it is respectfully requested that the Examiner telephone the undersigned so that further examination of this application can be expedited.

Respectfully submitted,

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